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09/935,316	08/22/2001	Ching-Leou Teng	ISIS-4824	1463

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/935,316	TENG ET AL.	
	Examiner	Art Unit	
	J. E. Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/14/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is in response to Applicant's submission filed on 8/14/2008.

Claims 30-58 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Specification

The amendment filed 8/14/2008 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the new text added to paragraph [0124].

It is noted that applicants argue that the new material can be added because the specification has incorporated by reference the source for the new text. It is acknowledged that Applicants have incorporated by reference the source for the new text. However, the instant insertion of new text, which is essential material, into the specification by reference to a publication is improper because 37 CFR 1.57(c) states:

> (c) **"Essential material"** may be incorporated by reference, but only by way of an incorporation by reference to a **U.S. patent or U.S. patent application publication**, which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material" is material that is necessary to:
>
> (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112;

(2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or

(3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112. (Emphasis added)

Which is in contrast to 37 CFR 1.57(d) which states:

(d) Other material **("Nonessential material")** may be incorporated by reference to U.S. patents, U.S. patent application publications, foreign patents, foreign published applications, prior and concurrently filed commonly owned U.S. applications, or **non-patent publications**. An incorporation by reference by hyperlink or other form of browser executable code is not permitted. (Emphasis added)

With respect to "Essential material", it is noted that MPEP § 608.01(p) states:

"Essential material" is defined >in 37 CFR 1.57(c)< as that which is necessary to (1) **>provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112, (2) describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112, or (3) describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112. **In any application that is to issue as a U.S. patent, essential material may only be incorporated by reference to a U.S. patent or patent application publication.** (Emphasis Added).

In the instant case, the amendment to ¶[0124] is considered essential because it is necessary to provide a written description of the claimed invention, and of the manner and

process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the reply to this Office Action or to resubmit the amendment with the appropriate affidavit or declaration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

MPEP §2163.06 notes:

If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.02 teaches that:

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

MPEP §2163.06 further notes:

When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

As previously indicated, claims 48 and 54 include the limitation that the capsule is a single compartment capsule (Emphasis added). Applicants have pointed to amended paragraph 0124 of the specification as support for the limitation "single compartment capsule". However, as indicated above, the amendment to paragraph 0124 has not been entered. As such, the version of paragraph 0124 prior to the non-entered amendment was closely reviewed by the Examiner, however, neither explicit, implicit nor inherent support for a "single compartment capsule" was found in this paragraph 0124, or anywhere else in the specification, as previously indicated.

Briefly, instant paragraph 0124 does not contemplate using the species which is a single compartment capsule. Since the disclosure of a broad genus does not anticipate every species which it encompasses, the disclosure of paragraph 0124 does provide proper support for a single compartment capsule.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, the instant claims are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 30-36, 38-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,877,309 (McKay et al.) in view of US Patent 5,508,040 (Chen, cited by Applicants) and US Patent 5,840,329 (Bai, cited by Applicants).

McKay teaches a method which comprises administering to a human a composition comprising a drug that is an antisense oligonucleotide (e.g., column 6, lines 29-65); wherein the

antisense oligonucleotide is comprised in a formulation for oral delivery which can comprise a polyacrylic polymer, such as capric acid and polyacrylates (e.g., see: col. 20, lines 52-54; col.22, lines 4-19; col. 23, lines 24-40; col. 25, lines 1-7; and col. 28, lines 3-4). McKay teaches that the therapeutic formulation can be comprised in a capsule or tablet (e.g., see column 22, lines 49-60). Additionally, McKay teaches that the antisense drug composition can comprise hydroxypropylmethylcellulose and polyacrylates (e.g., see col. 23, lines 29-40). McKay also teaches that the formulation which comprises the second population of carriers can further comprise an enteric coating (e.g., see column 20,line 43 through column 21, line 4; also see column 23, lines 24-48).

McKay does not particularly teach that the formulation is made such that the first and second populations of carriers are arranged such that intestinal tissue is activated by the penetration enhancer prior to arrival of the drug such as by using a formulation that is specifically made by making the first population of carriers and then preparing the second population of carriers and then combining the two populations of carrier particles.

However, it was well recognized in the art at the time the invention was made that controlled release formulations can provide timed release of therapeutic agents. For example, both Chen and Bai. Chen teaches unit dosage forms for drugs or therapeutic agents that will release the drug in a series of sequential, pulsatile releasing events. The dosage form may be arranged to resist dissolution in certain environments such as enteric coated tablets which will not release pellets until they have passed the stomach. Chen teaches at column 5 that in one embodiment of the invention a two pulse dosage unit is comprised of one population of coated pellets and another population of pellets that do not have a delayed release coating to promptly

provide the first pulse while the second pulse is delayed by the special coating on the first population of pellets. Chen further teaches at column 3 the inclusion of penetration enhancers such as fatty acids. Bai teaches a pre-programmed drug delivery system consisting of a plurality of particles comprising individual delivery units that release the active agent and which can deliver a therapeutic agent over a period of time. The delivery system is able to deliver single agent or multiple agents simultaneously or sequentially, in any desired pattern with predetermined timings of pulse release from, and predetermined pulse duration of, individual delivery units. Furthermore, Bai teaches preparing the formulation by making the one population of particles and then the other population of particles and combining the two populations to make the desired pulsatile releasing formulation (e.g., see column 11, line 28 through column 12, line 10).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of McKay, Chan, and Bai to create the instantly claimed method with a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to combine the references to create claimed invention because McKay does not particularly teach how to make the formulation for delivery of the oligonucleotide to the intestines, while Chen and Bai provide more specific guidance on making pulsatile releasing formulations. Furthermore, Chen provides specific motivation by teaching that pulsatile release of therapeutic agents will increase resistance dissolution; and Bai provides motivation by teaching that it is desirable to deliver a therapeutic agent over a period time.

2. Claims 30, 33 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,877,309 (McKay et al.) in view of US Patent 5,508,040 (Chen, cited by Applicants) and US Patent 5,840,329 (Bai, cited by Applicants), and further in view of US Patent 5,514,788 (Bennett et al.).

It is noted that McKay, Chan and Bai together teach a method for enhancing the intestinal absorption of an antisense drug in an animal, comprising administering to the animal a formulation comprising: (a) a first population of carrier particles comprising an drug-bioadhesive component, wherein the drug is an antisense oligonucleotide; and (b) a second population of carrier particles comprising a penetration enhancer, wherein the formulation is made such that the first and second populations of carriers are arranged such that intestinal tissue is activated by the penetration enhancer prior to arrival of the drug such as by using a formulation that is specifically made by making the first population of carriers and then preparing the second population of carriers and then combining the two populations of carrier particles, as indicated above.

McKay, Chan and Bai do not teach that the oligonucleotide comprises SEQ ID NO: 1.

However, Bennett teaches an antisense oligonucleotide that exactly matches SEQ ID NO: 1 of the instant claims (see SEQ ID NO: 22 in column 35 of Bennett) wherein the antisense oligonucleotide can be used administered to an animal for a method of treatment (e.g., see abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of McKay, Chan, and Bai with the

teachings of Bennet to make the claimed method wherein the drug is an antisense oligonucleotide comprising SEQ ID NO: 1 (i.e., the antisense oligonucleotide taught by Bennet) with a reasonable expectation of success.

The motivation to make the modification is provide in part by both McKay and Bennett. Specifically, McKay teaches a method for administering a therapeutic antisense oligonucleotide to an animal and Bennett teaches a specific therapeutic antisense oligonucleotide comprising SEQ ID NO: 1.

Response to Arguments

3. Applicant's arguments filed 8/14/2008 have been fully considered but they are not persuasive.

With respect to Applicants' arguments regarding the incorporation of essential subject matter, including the reference to 37 CFR 1.57(g), Applicant is respectfully reminded that 37 CFR 1.57(g) does not explicitly indicate that essential subject matter can be entered when the reference is not a U.S. Patent or published application. 1.57(g) only states that incorporation of Essential subject matter may be entered, but only prior to close of prosecution or abandonment. Furthermore, the other arguments that the amendment should be entered, it is noted that applicants arguments would be persuasive if the subject matter were not essential. However, since the subject matter is essential, the only reference which may be relied upon for incorporation by reference of essential subject matter is a U.S. Patent or a published U.S. Application. Since this not the case here, Applicants arguments are not persuasive.

With respect to Applicants arguments regarding the New Matter rejection as it pertains to the use of a single compartment capsule, it is respectfully pointed out that the disclosure contemplates a genus of different types of capsules and limiting the claims to a specific species requires that the species be clearly disclosed. However, in the instant case, the disclosure does not clearly disclose the use of a single compartment capsule. With respect to arguments regarding the preparation limitation(s), Applicants arguments are persuasive and the rejection as it applies to this particular embodiments is withdrawn.

With respect to Applicants argument regarding the 103 rejection, it is noted that both Chen and Bai both provide motivation to make pulsatile releasing formulations. It is noted that the teachings of Chen and Bai were stated in the previous rejection and the explicit reference to those teachings is now made clear. Furthermore, it is noted that the *KSR* decision forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, --USPQ2d--, slip. op at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR,* USPQ2d at 1396) (available at http://www.USPTO.gov/web/offices/dcom/bpai/prec/fd071925.pdf).

Furthermore, in the Supreme Court decision in *KSR International CO. v. TELEFLEX INC.,* No. 04-1350 (U.S. Apr. 30, 2007), at page 17, the Court expressed "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense." (Emphasis added). Also, at page 13, the Court stated, "If a person of ordinary skill can implement a predictable variation, §103 likely

bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill."

In view of the foregoing, since there was a design need to increase stability of therapeutic drug for oral delivery to the intestines, and since there were a finite number of identified modifications to the delivery composition to enhance delivery to the intestines that were known, and since the skills required to make the modified delivery composition were within the technical grasp of one of ordinary skill in the art, and the prior art specifically taught pulsatile release is one technique to improve delivery (e.g., Chen and Bai) the claimed invention would have been *prima facie* obvious at the time of filing.

Therefore, Applicants arguments are not persuasive.

Conclusion

No claim is allowed.

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner, Art Unit 1635